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TITLE:

Targeting Histone Abnormality in Triple-Negative Breast Cancer

PRINCIPAL INVESTIGATOR:

Yi Huang, M.D., Ph.D.

CONTRACTING ORGANIZATION:

University of Pittsburgh, Pittsburgh, PA 15213

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6. AUTHOR(S)
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5d. PROJECT NUMBER
N/A

5e. TASK NUMBER
N/A

5f. WORK UNIT NUMBER
N/A

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
University of Pittsburgh Cancer Institute,

204 Craft Ave, Room A406,Pittsburgh,

8. PERFORMING ORGANIZATION REPORT NUMBER
N/A

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Materiel Command
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13. SUPPLEMENTARY NOTES
N/A

14. ABSTRACT In the first funding year, we tested our hypothesis that silencing of key tumor suppressive genes by enhanced crosstalk between LSD1 and HDACs is a unique epigenetic mechanism promoting TNBC growth, and blockade of the LSD1/HDAC axis results in profound inhibition of TNBC growth and metastasis, mediated at least in part via induction of RGS16. We demonstrated that HDAC5 physically interacted with LSD1 complex through NLS domain, and promoted LSD1 protein stability through upregulating LSD1-specific deubiquitinase USP28. Increased cellular proliferation mediated by HDAC5 overexpression was diminished by LSD1-KD, suggesting a critical role of LSD1 in regulating oncogenic activity of HDAC5. By using MCF10A TNBC tumor progression model, we observed that HDAC5-LSD1 axis possesses a critical oncogenic function in driving breast cancer development. Moreover, teams of the two PIs collaborated to study the combinatorial effect of natural HDAC inhibitor sulphoraphane and novel LSD1 inhibitor HCI-2509 on growth of MDA-MB-231 cells using xenograft model. These new findings provide solid evidence to suggest that crosstalk between LSD1 and HDACs represents a rational target for the development of drugs that can block their activity in TNBC cells.

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			19b. TELEPHONE NUMBER *(include area code)*
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1. INTRODUCTION

Triple negative breast cancer (TNBC) is the most aggressive subtype of breast cancer and lack of specific targets for TNBC patients remains a major clinical challenge. Therefore, new targeted approaches are urgently needed to improve TNBC treatment and prevention. Our early published work has provided novel insights into molecular mechanisms of a unique alteration of gene expression pattern as a result of dysregulated interaction between HDAC5 and LSD1 that could promote the TNBC initiation and progression. This funded Breast Cancer Breakthrough Award is a partnership between Dr. Yi Huang (initiating PI) and Dr. Nancy E. Davidson (partner PI). In the first funding year, the two labs have been closely working together using multiple *in vitro* and *in vivo* models to decipher how to apply novel epigenetic agents in the most favorable combination strategy against TNBC and investigate how epigenetic changes might contribute directly to TNBC tumorigenesis. To study the role of LSD1/HDACs axis in promoting transformation of TNBC (**Aim 1A**), gain- and loss-of-function of MCF10A progression model was used. We observed that HDAC5 possessed a critical oncogenic function in driving TNBC development through blocking LSD1 protein degradation and re-shaping epigenetic landscape. Our studies also revealed that HDAC5 physically interacts with LSD1 and stabilizes LSD1 protein level through posttranslational modification in TNBC cells. In addition, we further elucidated the role of RGS16 signaling pathway in LSD1-mediated HDACi efficacy in TNBC (**Aim 1B**). By using quantitative ChIP analysis, we have demonstrated that shRNA-HDAC5 significantly decreased the occupancy of HDAC5/LSD1 complex and increased the levels of AcH3K9 and H34me2 at the promoter of RGS16. In the next funding year, the Huang and Davidson labs will continues to work together to explore the precise mechanisms of HDAC5-LSD1 pathway in TNBC development and evaluate the therapeutic effect of inhibition of HDAC5-LSD1 axis in prevention and therapy of TNBC.

2. KEYWORDS

Breast cancer, HDAC5, LSD1, USP28, sulforaphane, combination therapy

3. ACCOMPLISHMENTS

a. What were the major goals of the project?

The hypothesis for our work is that silencing of key tumor suppressive genes by enhanced crosstalk between LSD1 and HDACs is a unique epigenetic mechanism promoting TNBC growth and metastasis, and blockade of the LSD1/HDAC axis results in profound inhibition of TNBC growth and metastasis, mediated at least in part via induction of RGS16. This is to be addressed through three specific aims:

1. Delineate the molecular basis by which inhibition of LSD1 promotes HDACi-induced apoptosis through reactivation of aberrantly silenced tumor suppressor genes.
2. Elucidate the role of LSD1 in HDACi therapy and chemoprevention of TNBC in animal models.
3. Evaluate therapeutic effects of combination strategies in patient-derived xenografts (PDXs).

b. What was accomplished under these goals?

Proposed Aims	Accomplishment

Specific Aim 1: Delineate the molecular basis by which inhibition of LSD1 promotes HDACi-induced apoptosis through reactivation of aberrantly silenced tumor suppressor genes.	The Huang lab, in collaboration with Davidson lab, investigated whether LSD1/HDAC crosstalk promotes TNBC pathogenesis. Our studies provided solid evidence showing that an orchestrated interplay between HDAC5 and LSD1 is a fundamental epigenetic mechanism contributing to TNBC proliferation and metastasis.
Major Task 1: Determine the role of LSD1/HDACs axis in promoting tumorigenic transformation of TNBC.	
Subtask 1: Submit IRB approval for use of LSD1/HDAC expression plasmids. (Month 1-2)	The proposed work was approved by University of Pittsburgh Institutional Review Board (PRO14030148, 3/10/2014).
Subtask 2: Establish MCF-10A cells with overexpression of LSD1, HDAC1, HDAC5 or combination. (Month 3-6)	We generated two MCF-10A cell lines stably overexpressing HDAC5 (MCF10A-HDAC5). Overexpression of HDAC5 in MCF10A cells increased LSD1 protein level and promoted cell proliferation of both HDAC5-KD clones (**Fig. 1A & B**), indicating a growth-promoting role for HDAC5 in MCF10A cells.
Subtask 3: Treat transfected MCF-10A cells for 6 months with mutagen ICR191 and test the potential transformation of transfected MCF-10A cells in 3D culture (Month 7-15).	Vector control and HDAC5 overexpressing MCF-10A cells were cultured for 7 months in growth medium containing ICR191. Soft agar colony formation study demonstrated that ICR191 treatment improved the ability of MCF10A cells to form growing colonies in soft agar, and overexpression of HDAC5 significantly promoted ICR191 induced colony formation in MCF10A cells, suggesting that HDAC5-LSD1 axis has the capacity to facilitate tumorigenic transformation induced by genomic instability in TNBC (**Fig. 1C**).
Major Task 2: Elucidate the role of RGS16 signaling pathway in LSD1-mediated HDACi efficacy in TNBC.	
Subtask 1: Stable knockdown of RGS16 expression in MCF-10A cells.	The generation of stable MCF-10A-RGS16-KD cell line is in progress. In addition, by using quantitative ChIP analysis, we have demonstrated that shRNA-HDAC5 significantly decreased the occupancy of HDAC5/LSD1 complex and increased the levels of AcH3K9 and H34me2 at the promoter of RGS16 (**Fig 2**).This result suggests that HDAC5/LSD1 complex plays an important role in governing the activities of key histone marks such as H3K4me and AcH3K9 at RGS16 promoter that may lead to the abnormal suppression of RGS16 transcription activity in breast cancer cells.
Subtask 2: Evaluate whether silencing of RGS16 promotes MCF-10A tumorigenesis (Month 5-8).	Once the stable MCF-10A-RGS16-KD cell line is successfully generated, we will test the effect of RGS16 inhibition on MCF-10A cell tumorigenesis.

Other reportable results	We have demonstrated that the interaction between LSD1 and HDAC5 stabilized LSD1 protein (**Fig. 3A & 3B**). Ubiquitination assays in MDA-MB-231 cells showed that HDAC5 overexpression significantly decreased LSD1 polyubiquitination (**Fig. 3C**). HDAC5 stabilizes LSD1 protein through upregulation of USP28, a specific deubiquitinase for LSD1 (**Fig. 3D**). These findings support the notion that interaction of HDAC5 and LSD1 stabilizes LSD1 protein via blockade of LSD1 proteasomal degradation. Simultaneous overexpression of USP28 prevented the destabilization of LSD1 by HDAC5 siRNA without altering HDAC5 protein expression (**Fig. 3E**). Together, these results suggested that HDAC5 acted as a positive LSD1 regulator through stabilization of USP28 protein expression and activity.

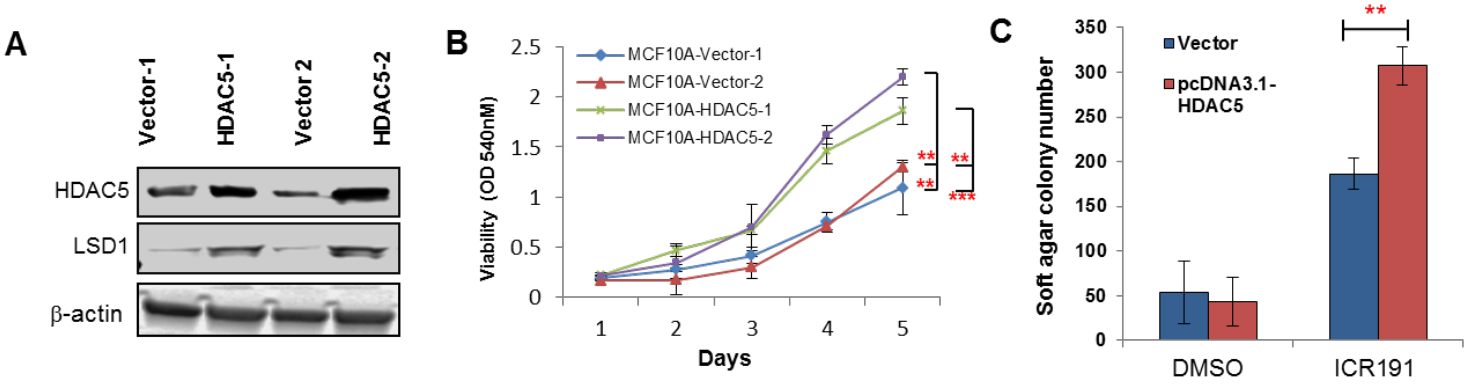

Figure 1. Effect of HDAC5 on growth and mutagen-induced tumorigenic transformation in MCF10A cells. (A) MCF10A cells were transfected with pcDNA3.1-HDAC5 plasmid followed by immunoblots with anti-HDAC5 and anti-LSD1. (B) Crystal violet assay for growth of MCF10-A stably transfected with empty or pcDNA3.1-HDAC5 plasmids. (C) MCF10A cells transfected with pcDNA3.1 or pcDNA3.1-HDAC5 plasmids were treated with 500ng/ml ICR191 for 7 months followed by soft agar colony formation assays. Bars represent the means of three independent experiments ± SD. ** p<0.01, **p<0.001 (Student's t-test).

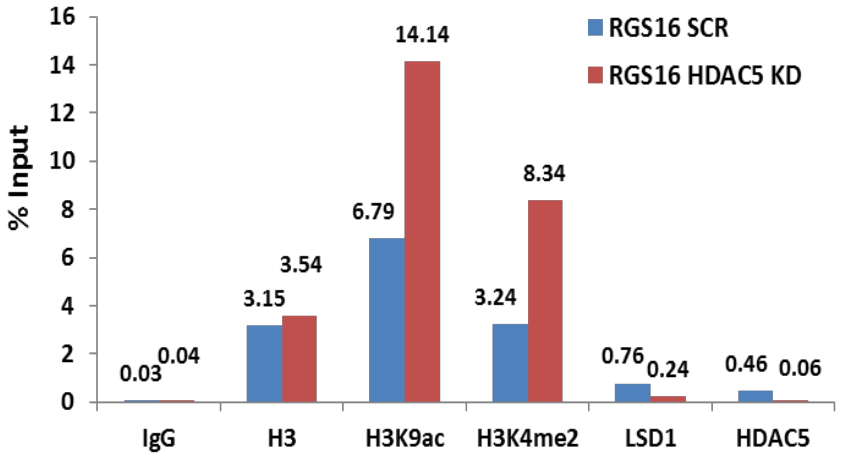

Figure 2. Stable knockdown of HDAC5 decreases the occupancy of HDAC5/LSD1 complex and increased the levels of AcH3K9 and H34me2 at the promoter of RGS16. Quantitative ChIP analysis was used to determine the occupancy of the RGS16 promoters by HDAC5, LSD1, H3K4me2 and acetyl-H3K9. IgG was used as a negative control.

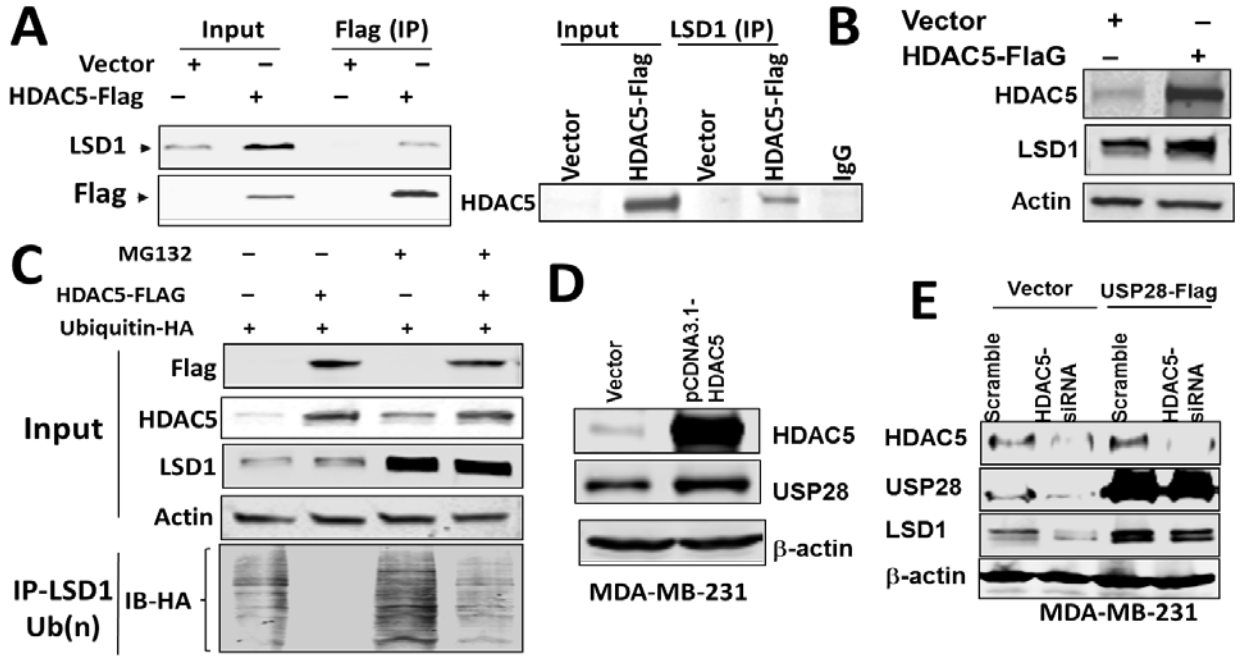

Figure 3. **HDAC5 interacts with and stabilizes LSD1 in breast cancer cells. (A)** MDA-MB-231 cells were transfected with control Flag vector or pCDNA3.1-HDAC5-Flag, and IP was performed with anti-Flag followed by IB with anti-LSD1 and anti-Flag, respectively (left panel). The co-IP was also performed with anti-LSD1 followed by IB with anti-HDAC5. Anti-rabbit IgG was used as negative control (right panel). **(B)** Overexpression of HDAC5 enhanced LSD1 protein expression in MDA-MB-231 cells. **(C)** MDA-MB-231 cells stably transfected with ubiquitin-HA expression vectors, control Flag vector or pCDNA3.1-HDAC5-Flag were treated with or without proteasome inhibitor MG132. Cellular extracts were immunoprecipitated with LSD1 antibody and the polyubiquitination of LSD1 was examined by immunoblotting using anti-HA antibody. **(D)** Overexpression of HDAC5 increased USP28 protein expression. **(E)** MDA-MB-231 cells were simultaneously transfected with HDAC5 siRNA and pDZ-Flag-USP28 for 48 h and whole cell lysates were analyzed for protein expression of HDAC5, USP28 and LSD1.

Proposed Aims	Accomplishment
Specific Aim 2: Elucidate the role of LSD1 in HDACi therapy and chemoprevention of TNBC in animal models.	Dr. Huang's team assisted Dr. Davidson's team in designing and performing the animal studies.
Major Task 4: Evaluate in vivo therapeutic effects of combination strategies using LSD1 inhibitors and HDACi in different subtypes of breast tumors.	
Subtask 1: Submit documents for local IACUC review (Month 6-8).	The research proposal has been approved by The University of Pittsburgh's Institutional Animal Care and Use Committee (Protocol #: 14033448, 3/24/2014, PI: Davidson).

Subtask 2: Examine the *in vivo* effects of LSD1/HDAC signaling on tumorigenic transformation of MCF-10A cells (Month 8-16).	We are currently evaluating the role HDAC5/LSD1 in breast tumorigenesis using MCF10A-HDAC5-KD cell line model. If the results obtained from these studies suggest that overexpression of LSD1/HDAC5 promotes tumorigenic transformation of MCF-10A cells, we will validate the *in vitro* results in MCF-10A xenograft-bearing mice.
Subtask 3: Evaluate combination strategies using LSD1i and HDACi in different subtypes of breast tumors (Month 10-26).	We investigated the potential effect of HDAC inhibitors on activity of HDAC5-LSD1 axis. We first tested a panel of HDAC inhibitors for their ability to affect HDAC5-USP28-LSD1 signaling pathway, and found that sulforaphane, a natural HDAC inhibitor found in cruciferous vegetables, significantly inhibited mRNA expression of HDAC5 without changing mRNA levels of LSD1 and UPS28 in MDA-MB-231 cells (**Fig. 4A**). Immunoblot studies indicated that sulforaphane, but not other HDACis, significantly downregulated protein expression of HDAC5 and LSD1 (**Fig. 4B**), and ubiquitination assays showed that treatment with sulforaphane in MDA-MB-231 cells increased LSD1 polyubiquitination (**Fig. 4C**), suggesting that sulforaphane might destabilize LSD1 through inhibition of HDAC5 expression. To confirm this hypothesis, we performed a rescue expression of HDAC5 cDNA in MDA-MB-231 cells through transfection of CMV promoter driven pCDNA3.1 vector that lacked any 5'-HDAC5 promoter sequence. QPCR test indicated that sulforaphane failed to suppress exogenous HDAC5 mRNA expressed driven by CMV promoter **(Fig. 4D**). This result thereby validated that sulforaphane downregulated HDAC5 mRNA level through repression of transcriptional activities at the native HDAC5 promoter. Immunoblot results indicated that sulforaphane exerted no effect on overexpressed HDAC5 protein and drug-mediated downregulation of USP28 and LSD1 protein was obviously reversed (**Fig. 4E**). We further studied whether overexpression of HDAC5 impeded cellular response to growth inhibition by sulforaphane. We demonstrated that MDA-MB-231 cells transfected with HDAC5 expression plasmid were more resistant to sulforaphane mediated growth inhibition which was evidenced by significantly increased IC_{50} value in both cell lines (**Fig. 4F**). Taken together, these results clearly suggest that HDAC5 acts as a critical regulator of antineoplastic activity of sulforaphane. We assisted the Davidson lab to test the *in vivo* c effect of sulforaphane alone or in combination with the LSD1 inhibitor, HCI-2509, using MDA-MB-231 xenografts in athymic nude mice. Treatment with either sulforaphane or HCI-2509 alone significantly inhibited growth of MDA-MB-231 xenografts, and the combination was even more effective. (**See Dr. Davidson's report**).

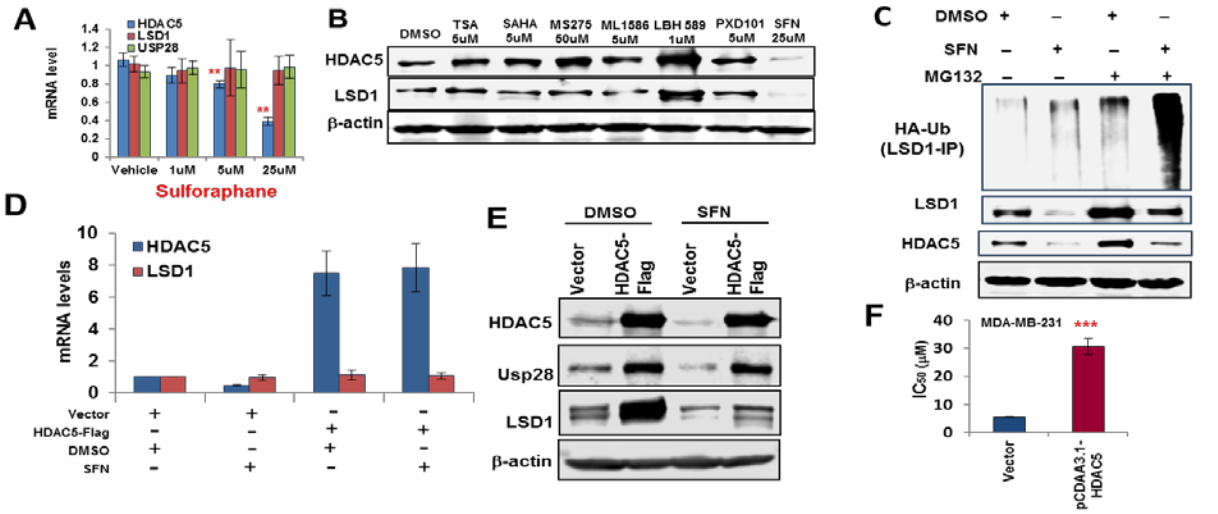

Figure 4. Sulforaphane inhibits activity of HDAC5-LSD1 axis. (A) After MDA-MB-231 cells were exposed to SFN for 24 h, mRNA was measured by quantitative PCR for mRNA expression of HDAC5, LSD1 and USP28. (B) MDA-MB-231 cells were exposed to HDAC inhibitors for 24 h. Whole cell lysate were analyzed for protein expression of HDAC5, and LSD1. β-actin was used as a loading control. (C) MDA-MB-231 cells were treated with 25 μM sulforaphane with or without proteasome inhibitor MG132 for 24 h. Cellular extracts were immunoprecipitated with LSD1 antibody and the polyubiquitination of LSD1 was examined by immunoblotting using anti-HA antibody. (D) MDAMB-231 cells stably transfected with pCDNA3.1 or pCDNA3.1-HDAC5-FLAG plasmids were treated with 25 μM sulforaphane for 24 h. mRNA was measured by quantitative real time PCR for indicated gene expression. (E) MDAMB-231 cells stably transfected with pCDNA3.1 or pCDNA3.1-HDAC5-Flag plasmids were treated with 25 μM sulforaphane for 24 h. Protein expression of HDAC5, USP28 and LSD1 was analyzed. (F) Cells were transiently transfected with pCDNA3.1-HDAC5 flag plasmids and simultaneously treated with 25 μM sulforaphane for 48 h. Cell proliferation was analyzed by crystal violet assays.

c. What opportunities for training and professional development has the project provided?

This award provides an excellent vehicle for a postdoctoral fellow, Chunyu Cao, Ph.D., working on this project to advance his breast cancer research career and transition to an independent position.

d. **How were the results disseminated to communities of interest?**

We presented this work at 2015 annual meeting of the American Association of Cancer Research (AACR): Cao C, Vasilatos S, Oesterreich S, Davidson NE, Huang Y. Functional crosstalk between histone deacetylase 5 (HDAC5) and lysine-specific demethylase 1 (LSD1) as a novel therapeutic target in triple-negative breast cancer cells. The 106th AACR Annual Meeting, Philadelphia PA, Cancer Res, Abstract#: 3838, 2015.

This work was also presented in at the annual retreats of the University of Pittsburgh Cancer Institute and Women's Cancer Research Center at the University of Pittsburgh.

One manuscript has been submitted to *Oncogene* for publication and it is currently under revision.

e. What do you plan to do during the next reporting period to accomplish the goals?

During the next reporting period, we plan to: (1) continue to elucidate the role of HDAC5 and LSD1 in regulation of TNBC initiation and transformation (**Aim 1A**). We will investigate whether synchronized gain-of-function of HDAC5 and LSD1 facilitates TMBC tumorigenesis. (2) explore the mechanism by which RGS16 reactivation enhances HDACi-induced apoptosis (**Aim**

1B). (3) continue to study how HDAC5 stabilizes LSD1 protein and promotes LSD1 activity in TNBC cells. We will define the mechanisms underlying the regulation of HDAC5 on posttranslational modification of LSD1 protein. We will further characterize how the interplay between HDAC5 and USP28 regulates LSD1 protein stability. (4) characterize the biological function of newly identified genes regulated by crosstalk between HDAC5 and LSD1 (**Aim 1C**).

4. IMPACT

(a) What was the impact on the development of the principal discipline(s) of the project? Our new findings in the first funding year have opened a new avenue for the potential utility of crosstalk between HDAC5 and LSD1 as a novel epigenetic target for poorly differentiated and aggressive TNBC, which is an important research area that has been understudied in invasive breast cancer. The information derived from these studies will likely validate whether the new subset of aberrantly silenced tumor suppressor genes governed by HDAC5-LSD1 axis has potential to serve as a novel panel of therapeutic biomarkers to predict or indicate the response to epigenetic therapy in TNBC patients. Targeted HDAC5 inhibition with the natural product, sulforaphane, in combination with a newly developed potent LSD1 inhibitor HCI-2509 showed superior antineoplastic activity both *in vitro* and *in vivo*. The ongoing study will seek to uncover how the HDAC5-LSD1 axis contributes to resistance to HDACi therapy in breast cancer. The information gained from this study could lead to validation and translation of our new strategy into future trials.

(b) What was the impact on other disciplines? Nothing to Report

(c) What was the impact on technology transfer? Nothing to Report

5. CHANGES/PROBLEMS

(a) Changes in approach and reasons for change

No major changes in approach have been made since the initiation of the award.

(b) **Actual or anticipated problems or delays and actions or plans to resolve them**

Nothing to Report

(c) **Changes that had a significant impact on expenditures**

Nothing to Report

(d) **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

The natural HDAC inhibitor sulforaphane and novel LSD1 inhibitor HCI-2509 have been added as new agents to study their ability in targeting HDAC5-LSD1 axis in breast cancer.

6. PRODUCTS

(a) Publications, conference papers, and presentations

Cao C, Vasilatos S, Oesterreich S, Davidson NE, Huang Y. Functional crosstalk between histone deacetylase 5 (HDAC5) and lysine-specific demethylase 1 (LSD1) as a novel therapeutic target in triple-negative breast cancer cells. The 106th AACR Annual Meeting, Philadelphia PA, Cancer Res, Abstract#: 3838, 2015.

One manuscript has been submitted to *Oncogene* for publication and it is currently under revision.

(b) **Website(s) or other Internet site(s)** Nothing to Report

(c) **Technologies or techniques** Nothing to Report

(d) **Inventions, patent applications, and/or licenses** Nothing to Report

(e) **Other Products** Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

a) Individuals who have worked on the project

Name:	Yi Huang	Nancy Davidson	Shauna Vasilatos	Chunyu Cao
Project Role:	Co-PI	Co-PI	Technician	Postdoc Fellow
Researcher Identifier (e.g. ORCID ID):	N/A	N/A	N/A	N/A
Nearest person month worked:	3.6	1.2	9.0	6.0
Contribution to Project:	Designed and oversaw the studies to define in depth the basic mechanisms and biological consequences of the functional interplay between HDAC5/LSD1 in breast cancer	Oversaw IHC studies and animal experiments, and interpreted the results generated from *in vivo* studies	Performed IHC and microarray studies, oversaw critical lab management activities	Studied molecular mechanisms by which LSD1 and HDAC interacted, and carried out animal study
Funding Support:	CDMRP Breast Cancer Breakthrough Award, Breast Cancer Research Foundation	CDMRP Breast Cancer Breakthrough Award, Breast Cancer Research Foundation	CDMRP Breast Cancer Breakthrough Award	CDMRP Breast Cancer Breakthrough Award

b) Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Dr. Tiffany Katz completed her postdoctoral fellow training, and Dr. Chunyu Cao joined the laboratory to carry out the work as a postdoctoral fellow.

c) What other organizations were involved as partners?

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: Partnering PI, Dr. Nancy E. Davidson, will submit her annual report separately.

QUAD CHARTS: N/A

9. APPENDICES: updated curriculum vitae is attached

CURRICULUM VITAE

University of Pittsburgh
School of Medicine

BIOGRAPHICAL

Name: Yi Huang

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EDUCATION and TRAINING

Date Attended	Name and Location of Institution	Degree Received and Year	Major Subject
Undergraduate			
1986-1991	Nanjing Medical University, Nanjing, China	M.D., 1991	Clinical Medicine
Graduate			
1996-2001	Medical University of South Carolina, Charleston, SC	Ph.D., 2001	Pathology and Lab Medicine
Postgraduate			
1991-1994	Affiliated Hospital of Medical College of Nanjing University, Nanjing, China	Residency	Surgery
2001-2005	Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University, Baltimore, MD	Postdoctoral fellow	Oncology

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APPOINTMENTS and POSITIONS

ACADEMIC:

Years Inclusive	Name and Location of Institution or Organization	Rank/Title
2006-2009	Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, MD	Research Associate (Faculty)
2009-2015	Department of Pharmacology and Chemical Biology, School of Medicine, University of Pittsburgh, Pittsburgh, PA	Research Assistant Professor
2010-2012	Cancer Therapeutics Program, University of Pittsburgh Cancer Institute, Pittsburgh, PA	Member
2012-	Womens Cancer Research Center, Breast and Ovarian Cancer Program, University of Pittsburgh Cancer Institute, Pittsburgh, PA	Member
2015-	Department of Pharmacology and Chemical Biology, School of Medicine, University of Pittsburgh, Pittsburgh, PA	Assistant Professor (tenure track)

MEMBERSHIP in PROFESSIONAL and SCIENTIFIC SOCIETIES

Organization	Year
The American Association for Cancer Research (Active Member).	1998-
The America Association for Advancement of Science	1999-2001, 2013-2015

HONORS

Honors and Awards	Year
1st Prize of 32nd Annual Research Day, Medical University of South Carolina.	1997
Young scholar award for the 8th International Symposium of SCBA in Hong Kong.	1999
DOD breast Cancer Postdoctoral Fellowship Award	2002
Hodson Young Investigator in Oncology, Johns Hopkins Sidney Kimmel Comprehensive Cancer Center.	2007
Invited lecturer of Gordon Research Conference on Polyamines	2009
Samuel and Winters Foundation award for Medical Research	2011

Competitive Medical Research Fund (UPMC) Award	2012
Director's award of basic science at UPCI annual retreat poster competition (senior author)	2013
DOD Breast Cancer Breakthrough Award	2014

PUBLICATIONS

I. Research Articles

1. **Huang Y**, Johnson KR, Norris JS, Fan W. NF-κB/IκB signaling pathway may contribute to the mediation of paclitaxel-induced apoptosis in solid tumor cells. *Cancer Res*., 60: 4426-4432, 2000. PMID: 10969788

2. **Huang Y** and Fan W. IκB Kinase activation is involved in the regulation of paclitaxel-induced apoptosis in human tumor cell lines. *Mol. Pharmacol*., 61: 105-113, 2002. PMID: 11752211

3. **Huang Y**, Fang Y, Dziadyk JM, Norris JS, Fan W. The possible correlation between activation of NF-κB/IκB pathway with the susceptibility of tumor cells to paclitaxel-induced apoptosis. *Oncology Res*., 13: 113-122, 2002. PMID: 12392159

4. **Huang Y**, Hager ER, Phillips DL, Dunn VR, Hacker A, Frydman B, Kink JA, Valasinas AL, Reddy VK, Marton LJ, Casero RA, Davidson NE. A novel polyamine analog inhibits growth and induces apoptosis in human breast cancer cells. *Clin. Cancer. Res*., 9: 2769-2777, 2003. PMID: 12855657 PMCID: PMC3625930

5. **Huang Y**, Fang Y, Wu J, Dziadyk JM, Zhu X, Sui M, Fan W. Regulation of vinca alkaloid-induced apoptosis by NF-κB/IκB pathway in human tumor cells. *Mol. Cancer Ther*. 3: 271-277, 2004. PMID: 15026547

6. **Huang Y**, Keen JC, Hager ER, Smith R, Frydman, B, Valasinas AL, Reddy VK, Marton LJ, Casero RA, Davidson NE. Regulation of polyamine analogue cytotoxicity by c-Jun in human cancer MDA-MB-435 Cells. *Mol. Cancer Res*., 2: 81-88, 2004. PMID: 14985464

7. **Huang Y**, Pledgie A, Rubin E, Marton LJ, Woster PM, Sukumar S, Casero RA, Davidson NE. Role of p53/p21$^{WAF1/CIP1}$ activation in the mediation of polyamine analogue induced growth inhibition and cell death in human breast cancer cells. *Cancer Biol. Ther*., 4(9):1006-1013, 2005. PMID: 16131835 PMCID: PMC3639297

8. Pledgie AM, **Huang Y**, Hacker A, Zhang Z, Woster PM, Davidson NE, Casero RA. Spermine oxidase SMO (PAOh1), not N^1-acetylpolyamine oxidase (PAO) is the primary source of cytotoxic H_2O_2 in polyamine analogue-treated human breast cancer cell lines. *J. Biol. Chem*., 280(48): 39843-39851, 2005. PMID: 16207710

9. **Huang Y**, Keen JC, Pledgie A, Marton LJ, Zhu T, Sukumar S, Park BH, Blair BG, Brenner K, Casero RA, Davidson NE. Polyamine analogues down-regulate estrogen receptor α expression in

human breast cancer cells. *J. Biol. Chem.*, 281(28): 19055-19063, 2006. PMID: 16679312 PMCID: PMC3623667

10. Abukhdeir AM, Blair BG, Brenner K, Karakas B, Konishi H, Lim J, Sahasranaman V, **Huang Y**, Keen JC, Davidson NE, Vitolo M, Bachman KE, Park BH. Physiologic estrogen receptor alpha signaling in non-tumorigenic human mammary epithelial cells. *Breast Cancer Res. Treat*., 99(1):23-33, 2006. PMID: 16541319

11. Babbar N, Hacker A, **Huang Y**, Casero RA. Tumor necrosis factor α induced spermidine/spermine N^1-Acetyltransferase (SSAT) through Nuclear Factor κB in non small cell Lung cancer cells. *J. Biol. Chem*., 281(34): 24182-24192, 2006. PMID: 16757480

12. **Huang Y**, Greene E, Stewart TM, Goodwin AC, Baylin SB, Woster PM, Casero RA. Inhibition of the lysine specific demethylase, LSD1, by novel polyamine analogues results in re-expression of aberrantly silenced genes. *Proc. Natl. Acad. Sci. USA*, 104(19): 8023-8028, 2007. PMID: 17463086; PMCID: PMC1857229

13. Sui M, **Huang Y**, Park BH, Davidson NE, Fan W. Estrogen receptor α mediates breast cancer cells resistance to paclitaxel through inhibition of apoptotic cell death. *Cancer Res.*, 67(11): 5337-5344, 2007. PMID: 17545614

14. Madar I, **Huang Y**, Ravert H, Dalrymple SL, Davidson NE, Isaacs JT, Dannals RF, Frost JJ. Detection and quantification of the evolution dynamics of apoptosis using the PET voltage sensor 18F-fluorobenzyl triphenyl phosphonium. *J. Nucl. Med.*, 50(5): 774-780, 2009. PMID:19372481

15. **Huang Y**, Stewart TM, Wu Y, Baylin SB, Marton LJ, Woster PM, Casero RA. Novel oligoamine analogues inhibit lysine-specific demethylase 1 (LSD1) and induce re-expression of epigenetically silenced genes. *Clin. Cancer Res*., 15:7217-7228, 2009. (Featured on journal cover, Editorial by: Grant S, Clinical Cancer Research,15:7111-7113, 2009) PMID: 19934284 PMCID: PMC2927136

16. Hahm ER, Lee J, **Huang Y**, Singh SV. Withaferin A suppresses estrogen receptor-α expression in human breast cancer cells. *Mol. Carcinogenesis*, 50(8):614-624, 2011. PMID: 21432907 PMCID: PMC3129407

17. Zhu Q, **Huang Y,** Marton LJ, Woster PM, Davidson NE, Casero RA. Polyamine analogues modulate gene expression by inhibiting LSD1/KDM1 and altering chromatin structure in human breast cancer cells. *Amino Acids*, 42:887-898, 2012. PMID: 21805138 PMCID: PMC3240695

18. Sharma SK, Hazeldine S, Crowley ML, Hanson A, Beattie R, Varghese S, Senanayake TMD, Hirata A, Hirata F, **Huang Y**, Wu Y, Steinbergs N, Murray-Stewart T, Bytheway I, Casero RA, Woster PM. Polyamine-based small molecule epigenetic modulators. *Med. Chem. Commun.*, 3:14-21, 2012. PMID: 23293738 PMCID: PMC3535317

19. Jin K, Kong X, Shah T, Penet MF, Wildes F, Sgroi DC, Ma XJ, **Huang Y**, Kallioniemi A, Landberg G, Bieche I, Wu X, Lobie PE, Davidson NE, Bhujwalla ZM, Zhu T, Sukumar S. HOXB7 renders breast cancer resistant to tamoxifen through activation of the EGFR pathway. *Proc. Natl. Acad. Sci. USA*, 109(8):2736-2741, 2012. PMID: 21690342 PMCID: PMC3286915

20. **Huang Y***, Vasilatos S, Boric L, Shaw PW, Davidson NE. Inhibitors of histone demethylation and histone deacetylation cooperate in regulating gene expression and inhibiting growth in human breast cancer cells. *Breast Cancer Res. Treat.*, 131:777-789, 2012. (*Corresponding author) PMID:21452019 PMCID:PMC3624096

21. Hu D, Zhou Z, Davidson NE, **Huang Y**, Wan Y. Novel insight into KLF4 proteolytic regulation in estrogen receptor signaling and breast carcinogenesis. *J. Biol. Chem*., 287(17):13584-13597, 2012. PMID: 22389506 PMCID: PMC3340146

22. Zhu Q, Jin L, Casero RA, Davidson NE, **Huang Y**. Role of ornithine decarboxylase in regulation of estrogen receptor alpha expression and growth in human breast cancer cells. *Breast Cancer Res. Treat.*, 136:57-66, 2012. PMID: 22976807 PMCID:PMC3715085

23. Zhou Z, Jing C, Zhang L, Takeo F, Kim H, **Huang Y**, Liu Z, Wan Y. Regulation of Rad17 turnover unveils an impact of Rad17-APC cascade in breast carcinogenesis and treatment. *J. Biol. Chem*., 18134-18145, 2013. PMID: 23637229 PMCID: PMC3689957

24. Shaw PG, Chaerkady R, Wang T, Vasilatos S, **Huang Y**, Van Houten B, Pandey A, Davidson NE, Integrated proteomic and metabolic analysis of breast cancer progression. *PLOS ONE*, 8(9):e76220, 2013. PMID: 24086712 PMCID: PMC3785415

25. Vasilatos SV, Katz TA, Oesterreich S, Wan Y, Davidson, NE, **Huang Y**. Crosstalk between Lysine-specific Demethylase 1 (LSD1) and histone deacetylases mediates antineoplastic efficacy of HDAC inhibitors in human breast cancer cells. *Carcinogenesis*, 34(6):1196-1207, 2013. PMID: 23354309 PMCID: PMC3670252

26. Katz TA, Vasilatos SV, Oesterreich S, Davidson, NE, **Huang Y**. Inhibition of histone demethylase, LSD2 (KDM1B), attenuates DNA methylation and increases sensitivity to DNMT inhibitor-induced apoptosis in breast cancer cells. *Breast Cancer Res. Treat.*, 146(1):99-108, 2014. PMID: 24924415

27. Nowotarski SL, Pachaiyappan B, Holshouser SL, Kutz CJ, Li Y, **Huang Y**, Sharma SK, Casero RA, Woster PM. Structure-activity study for (bis)ureidopropyl- and (bis)thioureidopropyldiamine LSD1 inhibitors with 3-5-3 and 3-6-3 carbon backbone architectures. *Bioorg. Med. Chem.*, 23(7):1601-12, 2015. PMID: 25725609 PMCID:PMC4396983

28. Cao C, Vasilatos S, Bhargava R, Fine J, Oesterreich S, Davidson NE, **Huang Y**. Functional Interaction of Histone Deacetylase 5 (HDAC5) and Lysine-specific Demethylase 1 (LSD1) Promotes Breast Cancer Progression. *Oncogene*, in revision.

II. Peer-Reviewed Review Articles

1. Fan W, Sui M, **Huang Y.** Glucocorticoids selectively inhibit paclitaxel-induced apoptosis: mechanisms and its clinical impact. *Curr. Med. Chem*., 11: 403-411, 2004. PMID: 14965221

2. **Huang Y**, Pledgie AM, Casero RA, Davidson NE. Molecular mechanisms of polyamine analogues in cancer cells. *Anti-Cancer Drugs*, 16(3): 229-241, 2005. PMID: 15711175

3. **Huang Y**, Nayak S, Jankowitz R, Davidson NE, Oesterreich S. Epigenetics in breast cancer-what's new? *Breast Cancer Res.*, 13(6):225, 2011. PMID: 22078060 PMCID: PMC3326545

4. Katz TA, **Huang Y**, Davidson NE, Jankowitz JC. Epigenetic reprogramming in breast cancer: from new targets to new therapies. *Annals of Medicine*, 46(6):397-408, 2014. PMID:25058177

III. Book Chapters

1. **Huang Y** and Davidson NE. Chapter 74: Breast cancer. In: *Principles of Molecular Medicine* (2nd ed). Runge, M., and Patterson, WC. (eds), Humana Press, p728-735, 2006.

2. **Huang Y,** Woster PM, Marton LJ, Casero RA, Polyamine analogues targeting epigenetic gene regulation. *Essays Biochem*, Portland press, 46:95-110, 2009. PMID: 20095972 PMCID: PMC3564236

3. **Huang Y,** Shaw PW, Davidson NE. Chapter 22: Inhibition of histone deacetylation. In: *Epigenetics Protocols II*, Tollefsbol, TO (ed.), Methods in Molecular Biology, vol. 791, Springer Science, 791:297-311, 2011. PMID:21913088

4. **Huang Y,** Woster PM, Marton LJ. Chapter 10: The design and development of polyamine-based analogues with epigenetic targets. In: *Polyamine Drug Discovery*, Woster, PM., and Casero, RA. (eds). Royal Society of Chemistry Drug Discovery Series No. 17, Thomas Graham House, p238-256, 2012.

IV. Published Meeting Abstracts (partial list)

1. Fan W, **Huang Y**, Miller MC, Norris JN, Willingham MC. Evidence of taxol-induced apoptotic cell death via a signaling pathway independent of cell cycle arrest. The 89th AACR Annual Meeting, New Orleans, LA, Proc. Amer. Assoc. Cancer Res. 39:191, 1998.

2. **Huang Y**, Johnson KR, Fan W. The possible involvement of NF-κB/IκB in glucocorticoid-mediated inhibition of paclitaxel-induced apoptosis in human solid tumor cells. The 90th AACR Annual Meeting, Philadelphia, PA. Proc. Amer. Assoc. Cancer Res. 40:783, 1999.

3. **Huang Y**, Hager ER, Phillips DL, Hacker A, Frydman B, Valasinas AL, Reddy VK, Marton LJ, Casero RA, Davidson NE. Conformationally constrained polyamine analogues and oligoamines inhibit growth and induce apoptosis in human breast cancer cells. The 93rd AACR Annual Meeting, San Francisco, CA, Proc. Amer. Assoc. Cancer Res. 43:90, 2002.

4. **Huang Y**, Hager ER, Phillips DL, Smith R, Keen J, Frydman B, Valasinas AL, Reddy VK, Marton LJ, Casero RA, Davidson NE. Regulation of Polyamine Analogue Cytotoxicity by c-Jun in Human Breast Cancer Cells. 94th AACR Annual Meeting, Washington DC. Proc. Amer. Assoc. Cancer Res. 44:311, 2003.

5. Sui M, **Huang Y**, Dziadyk J, Zhu X, Fan M. Glucocorticoids Selectively Inhibit Taxane-Induced Apoptosis through Regulation of NF-κB and cIAP in Human Breast Cancer Cells. The 94th AACR Annual Meeting. Proc. Amer. Assoc. Cancer Res. 44:538, 2003.

6. Pledgie AM, Wang Y, **Huang Y**, Hacker A, Woster PM, Casero RA, Davidson NE. Differential induction of human spermine oxidase (PAOh1/SMO) mRNA and activity in human breast cancer cell lines. The 95th AACR Annual Meeting, Orlando, Florida, Amer. Assoc. Cancer Res. 45:1224, 2004.

7. **Huang Y**, Pledgie AM, Frydman B, Valasinas AL, Reddy VK, Marton LJ, Woster PM, Casero RA, Davidson NE. Distinct roles of p53/p21$^{WAF1/CIP1}$ and JNK/Jun activation in the mediation of polyamine analogue induced growth inhibition and cell death in human breast cancer MCF-7 cells. Gordon Research Conference on Molecular Therapeutics of Cancer, New London, New Hampshire, 2004.

8. **Huang Y**, Keen JC, Pledgie AM, Frydman B, Valasinas AL, Reddy VK, Marton LJ, Woster PM, Casero RA, Davidson NE. Estrogenic regulation of polyamine analogues in human breast cancer cells. The 96th AACR Annual Meeting, Los Angeles, CA, Proc. Amer. Assoc. Cancer Res. 46:547, 2005.

9. **Huang, Y**, Greene, E, Stewart, T.M., Goodwin, A.C., Baylin, S.B., Woster, P.M., and Casero, R.A., Jr. Reexpression of aberrantly silenced genes by novel polyamine analogues through inhibition of lysine specific demethylase (LSD1) in human colon carcinoma cells. Gordon Conference on Polyamines, Waterville Valley, NH, 2007.

10. **Huang, Y.**, Greene, E, Stewart, T.M., Goodwin, A.C., Baylin, S.B., Woster, P.M., and Casero, R.A., Jr. Re-expression of aberrantly silenced genes resulting from Inhibition of lysine-specific demethylase 1 (LSD1) by polyamine analogues in human colon cancer cells. The 235th ACS National Meeting, New Orleans, LA, 2008.

11. Stewart, T.M., **Huang, Y.**, Woster, P.M., and Casero, R.A., Jr. Polyamine analogue inhibition of lysine-specific demethylase 1 in human acute myeloid leukemia cell lines. The 99th AACR Annual Meeting, San Diego, CA, Proc. Amer. Assoc. Cancer Res. 46:2605, 2008.

12. **Huang, Y.**, Stewart, T.M., Marton L.J., and Casero, R.A., Jr. Novel oligoamine analogues inhibit lysine specific demethylase 1 and activate silenced gene re-expression in colon cancer cells. AACR special conference-Cancer Epigenetics, Boston, MA, 2008.

13. Hazeldine, S., Crowley M.L., **Huang, Y.**, Stewart, T.M., Casero, R.A., and Woster, P.M. Alkylamino- and alkylguanidinolysine analogue inhibitors of lysine-specific demethylase 1. The 236th ACS National Meeting, Philadelphia, PA, 2008.

14. **Huang, Y.**, Stewart, T.M., Wu, Yu, Marton L.J., Woster, P.M., and Casero, R.A., Jr. Novel oligoamine/polyamine analogues inhibit lysine-specific demethylase 1 (LSD1), induce re-expression of epigenetically silenced genes, and inhibit the growth of established human tumors *in vivo*. The 100th AACR Annual Meeting, Denver, CO, Proc. Amer. Assoc. Cancer Res. 47:#LB-173, 2009.

15. Zhu, Q., **Huang, Y.,** Casero, R.A., and Davidson, N.E. Knockdown of ornithine decarboxylase by siRNA suppresses ERα expression in human breast cancer cells. The 100th AACR Annual Meeting, Denver, CO, Proc. Amer. Assoc. Cancer Res. 47: 4426, 2009.

16. Zhu, Q., **Huang, Y.,** Marton L.J., Woster, P.M., Davidson, N.E. and Casero, R.A. Polyamine analogues modulate gene expression by inhibiting KDM1/LSD1 and altering chromatin structure in human breast cancer cells. The 101st AACR Annual Meeting, Washington, DC, 70(8 Suppl): 4877, 2010.

17. Shaw, P., Billam, M., Hood, B.L., **Huang, Y.,** Conrads, T.P., Davidson, N.E. Label free analysis of estrogen receptor (ER) negative tumors sensitized to tamoxifen by epigenetic therapy. The 58th ASMS Conference on Mass Spectrometry conference, Salt City, UT, May 23-27, 2010.

18. Stewart, T.M., **Huang, Y.**, Marton L.J., Belinsky, S.A., and Casero, R.A. Synergy between a histone deacetylase inhibitor and a polyamine analogue stimulates polyamine catabolism, modifies chromatin architecture, and induces re-expression of aberrantly silenced tumor suppressor genes. Gordon Research on Polyamines, Waterville Valley, NH, June 2011.

19. Van Houten B, Johnson A, **Huang Y**, Qian W, Barbi M. Regulation of mitochondrial respiration by 17β-estradiol through lactate dehydrogenase in MCF7 breast cancer cells. AACR Metabolism and Cancer, Baltimore, October 16-19, 2011.

20. Vasilatos SV, Katz TA, Oesterreich S, Davidson, NE, **Huang Y**. Breast cancer subtype-specific regulation of gene transcription and therapeutic response by functional crosstalk between LSD1 and HDACs. The 103rd AACR Annual Meeting, Chicago, IL, Cancer Res 2012; 72(8 Suppl): 1044, 2012.

21. Katz TA, Vasilatos SV, Oesterreich S, Chandran U Davidson, NE, **Huang Y**. Synergy between inhibition of novel histone demethylase (LSD2) and DNA methyltransferase (DNMT) and histone deacetylase (HDAC) in modulating gene expression and inhibiting growth in human breast cancer cells. The 103rd AACR Annual Meeting, Chicago, IL, Cancer Res; 72(8 Suppl):1052, 2012.

22. Christner SM, Clausen DM, Beumer JH, Parise RA, **Huang Y**, Dömling AS, Eiseman JL. Novel small molecule inhibitors of MDM2/4-p53 interaction, YH264 and its ethyl ester YH263: preclinical evaluation. The 103rd AACR Annual Meeting, Chicago IL, Cancer Res; 72(8 Suppl): 4726, 2012.

23. Vasilatos SV, Katz TA, Oesterreich S, Davidson, NE, **Huang Y**. Targeting LSD1-HDACs crosstalk as a potential therapeutic strategy for triple negative breast cancer cells. The 104th AACR annual Meeting; Washington, DC; Cancer Res; 73(8 Suppl): 673, 2013.

24. Katz TA, Vasilatos SV, Oesterreich S, Chandran U Davidson, NE, **Huang Y**. Inhibition of histone demethylase, LSD2, and DNA methyltransferase cooperates in reducing growth and modulating ERα expression in human breast cancer cells. Keystone meeting on Epigenetic Marks and Cancer Drugs, New Mexico, 2013.

25. Woodcock CS, Katz T, Davidson NE, Freeman BA, **Huang Y**. Therapeutics actions of electrophilic nitroalkenes via inhibition of the NF-κB pathway in triple negative breast cancer. 8th International Nitric Oxide Conference & 6th International Nitrite/Nitrate Conference, Cleveland, OH, Nitric Oxide 42: 106, 2014.

26. Woodcock C, Woodcock SR, Davidson NE, Freeman BA, **Huang Y**. Electrophilic nitroalkenes cause degradation of NF-κB/RelA in triple negative breast cancer cells. ASCB meeting, Bethesda, MD, Molecular Biology of the Cells, 25: 8120, 2014.

27. Cao C, Vasilatos S, Oesterreich S, Davidson NE, **Huang Y**. Functional crosstalk between histone deacetylase 5 (HDAC5) and lysine-specific demethylase 1 (LSD1) as a novel therapeutic target in triple-negative breast cancer cells. The 106th AACR annual meeting; Philadelphia, PA; Cancer Res; 75(15 Suppl): 3838, 2015.

∗**Total citations:** 1694 (Google scholar) ∗**Total journal impact factors:** 163.90 ∗**H-index:** 22 ∗**i10-index** 29 (as of 12/30/2015)

PROFESSIONAL ACTIVITIES

TEACHING

Mentoring

Postdoctoral fellows		Current position
2014-2016	Chunyu Cao, Ph.D.	Postdoc fellow, University of Pittsburgh

Doctoral Students

2015- Julia C. Woodcock, Pharmacology & Chemical Biology, University of Pittsburgh

Undergraduate Students

2010 Emily Platz
2015-2017 Lin Chen

High School Students

2013 Jennifer Han, UPCI Summer Academy
2015 Jeewon Lee, UPCI Summer Academy

Ph.D. Candidacy Exam Committee

2013 Courtney Anderson, Pharmacology & Chemical Biology, University of Pittsburgh
2013 Kyle Knickelbein, Pharmacology & Chemical Biology, University of Pittsburgh
2015 Nolan Priedigkeit, Pharmacology & Chemical Biology, University of Pittsburgh
2015 Alison Nagle, Pharmacology & Chemical Biology, University of Pittsburgh

Ph.D. Dissertation Committee

2013-present Julia C. Woodcock, Pharmacology & Chemical Biology, University of Pittsburgh

RESEARCH

1. Research Supports

Active Grant Support

Project number W81XWH-14-1-0237
Title: Targeting histone abnormality in triple negative breast cancer
Role in project: PI (Partnering PI: Davidson)
Year Inclusive: 8/1/2014-7/31/2017
Source: Department of Defense – Breast Cancer Program Breakthrough
Amount: $ 565,048

Project number
Title: Role of LSD2 in epigenetic gene silencing in breast cancer
Role in project: PI
Year Inclusive: 2013-2014
Source: UPCI Pilot Grant
Amount: $5,000

Project number BCRF0016554
Title: Role of histone demethylase in epigenetic regulation of gene expression in breast cancer
Role in project: Co-I, PI: Davidson
Year Inclusive: 2014-2015
Source: Breast Cancer Research Foundation
Amount: $200,000/yr ($70,279 supports Dr. Huang's research)

Prior Grant Support

Project number
Title: Targeting crosstalk between LSD1 and HDAC in triple negative breast cancer
Role in project: PI
Year Inclusive: 2012-2013

Source:	UPMC Competitive Medical Research Fund
Amount:	$25,000
Project number	P50 CA88843-08 (JHU PO#2009 12087) (Davidson)
Project number	BCRF0016554
Title:	Role of histone demethylase in epigenetic regulation of gene expression in breast cancer
Role in project:	Co-I, PI: Davidson
Year Inclusive:	2009-2014
Source:	Breast Cancer Research Foundation
Amount:	$89,418/yr
Title:	Specialized Program in Research Excellence (SPORE in Breast Cancer)
Role in project:	Co-I, PI of Project 2-2
Year Inclusive:	2009-2012
Source:	NCI
Amount:	$43,163/yr
Project number	
Title:	Crosstalk between histone demethylase and histone deacetylase: a novel epigenetic target for breast cancer
Role in project:	PI
Year Inclusive:	2011-2012
Source:	Samuel and Emma Winters Foundation
Annual direct cost:	$9,000
Project number	DAMD 17-03-1-0376 (Huang)
Title:	Antineoplastic efficacy of novel polyamine analogues in human breast cancer
Role in project:	PI
Year Inclusive:	2003-2006
Source:	DOD Breast Cancer Research Program
Amount:	$170,000
Project number	DAMD 17-00-1-0301 (Huang)
Title:	The role of histone deacetylase and DNA methylation in estrogen receptor expression in breast cancer
Role in project:	PI
Year Inclusive:	2002-2003
Source:	DOD Breast Cancer Research Program
Amount:	$96,000

Pending Grant Support

NCI RO1	Targeting HDAC5-LSD1 axis in triple negative breast cancer

2. Invited Seminars and Lectureships

2008.5. AACR special conference-Cancer Epigenetics, Boston, MA, "Novel oligoamine analogues inhibit lysine specific demethylase 1 and activate silenced gene re-expression in colon cancer cells."

2009.6. Polyamine Gordon conference, Waterville Valley, NH, "Histone Lysine-specific Demethylase (LSD1): an emerging epigenetic target for polyamine analogues in cancer therapy."

2009.9. The 1st UPCI Minisymposium on Biology, Treatment, and Prevention of Breast Cancer, Pittsburgh, PA, "Targeting epigenetic silencing in breast cancer: biology and translational implications".

2009.12. Pittsburgh Chromatin Club Symposium, Pittsburgh, PA. "Targeting histone lysine specific demethylase 1 (LSD1) as a novel epigenetic strategy in cancer therapy".

2010.5. University of Pittsburgh Cancer Institute Basic & Translational Research Seminar Series, Pittsburgh, PA. "Histone Lysine-specific Demethylase 1 (LSD1) as a potential therapeutic target for breast Cancer".

2011.9. The 1st Annual Retreat of Women's Cancer Research Center, University of Pittsburgh, "Epigenetics and breast cancer: exploding the box, or unraveling the chromatin"

2013.9. The 24th Annual Vascular Biology and Hypertension Symposium, University of Alabama at Birmingham, "Epigenetic regulation of estrogen receptor signaling in breast cancer: biology and therapeutic implications"

2015.10. The 4th International Breast Cancer Stem Cell Symposium, Suzhou, China, "Targeting Epigenetic Abnormality in Breast Cancer: Biology and Clinical Implication"

3. Invited Journal Peer Review Activities

- Amino Acids
- Breast Cancer Research
- Breast Cancer Research & Treatment
- BBA - Molecular Cell Research
- BMC Cancer
- Cancer Biology & Therapy
- Cancer Investigation
- Cancer Research
- Carcinogenesis
- Cell Death and Differentiation
- Clinical Cancer Research
- Clinical & Experimental Metastasis
- Cancer Letters
- Cell Biochemistry and Biophysics
- Frontiers of Epigenomics
- Hormones and Cancer
- Journal of National Cancer Institute
- Life Science
- Medicinal Chemistry Communications
- Molecular and Cellular Endocrinology

- Molecular Carcinogenesis
- Neoplasia
- Oncotarget
- PLOS ONE
- Reproductive Biology and Endocrinology
- Scientific Report
- The Journal of Investigative Dermatology
- Translational Oncology

4. Editorial Boards

2011-present	Frontiers in Epigenomics
2013-2015	Cancer and Clinical Research

5. Study Section or Scientific Review Services

2010	Panel reviewer, US Army/DOD Breast Cancer Research Program-Molecular Genetics & Biology
2015	Panel reviewer, US Army/DOD Breast Cancer Research Program- Breakthrough awards-Cell Biology
2015	Reviewer, Israel Science Foundation

SERVICE

University and Medical School Service

2000-01	President, International Association of Medical University of South Carolina
2013	Poster judge, 3rd Annual WCRC retreat, UPCI
2013	Poster judge, 24th Annual Vascular Biology and Hypertension Symposium, University of Alabama at Birmingham
2014	WCRC retreat planning committee
2014	UPCI retreat judge
2015	UPCI retreat organization committee member
2015-	UPCI Summer Academy, WCRC site director
2015	WCRC retreat judge
2016	2nd Great Lakes Breast Cancer Symposium organizing committee

Community Service

2000-01	Vice President, Association of Chinese Scholar and students of Charleston SC
2015.11.	Speaker, 2nd UPCI breast cancer advocacy boot camp